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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/400,492	09/21/1999	KENNETH RHODES	MNI-069CP	3470

959 7590 05/14/2004
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EXAMINER

MURPHY, JOSEPH F

ART UNIT PAPER NUMBER

1646

DATE MAILED: 05/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/400,492

Applicant(s)

RHODES ET AL.

Examiner

Joseph F Murphy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 11, 12, 15-19 and 24-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-3 and 25 is/are allowed.
- 6) ☒ Claim(s) 11-12, 15-19, 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 1-3, 11-12, 15-19, 24-26 are pending and under consideration.

Response to Arguments

Applicant's arguments filed 3/1/2004 have been fully considered but they are persuasive in part, for the reasons set forth below.

The rejection of claims 1-3, 25 under 35 USC § 112 first paragraph as lacking enablement has been withdrawn based on Applicant's arguments.

The rejection of claims 1-3, 25 under 35 USC § 112 first paragraph as lacking written description has been withdrawn based on Applicant's arguments.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-12, 15-19, 24 stand rejected, and new claim 26 is rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying a compound which binds to Kv4.2 or Kv4.3 and/or modulates the potassium channel activity of Kv4.2 or Kv4.3, does not reasonably provide enablement for a method of identifying a compound which binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel, or a method of identifying a compound which binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a biologically active PCIP polypeptide fragment, for reasons of record set forth in the Office Action of 10/30/2003. The specification does not enable

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any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue.

The rejection of record set forth that in the instant case, the claims are directed to a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel, or a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a biologically active PCIP polypeptide fragment. Since the claims are directed to methods using biologically active fragments of PCIP 9q polypeptides, the claims encompass methods using variant proteins. Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often

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destroy activity. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible fragments of PCIP 9q.

It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Thus, the amino acid sequence of a polypeptide determines its structural and functional properties, and predictability of which amino acids can be substituted is extremely complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the protein fragments are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims.

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to

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recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

In addition, the claims encompass a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel, without setting forth the activity of the Kv4.2 or 4.3 potassium channel that is to be modulated. Since the claims do not set forth a functional limitation which is modulated, it would require undue experimentation for the skilled artisan to determine the function which is to be modulated by the compound.

Given the breadth of claims 11-12, 15-19, 24, 26 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to practice the claimed invention.

Applicant argues that based on the teachings in the specification, an ordinary skilled artisan would be able to determine the function which is to be modulated by the test compound, and that Applicants provide working examples in which the activity of Kv4 potassium channels is monitored. However, the claims are directed to a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a biologically active PCIP polypeptide fragment. The term "biologically active" is not defined by the claims, and no definition is given as to what this activity is. Various biological activities can be attributed to a peptide. For example, "activity" could constitute transportation throughout a cell, alteration of tertiary structure due to changes in pH, ligand binding, or modulation of second messenger effect, etc. 'Activity' could also be referring to the ability of the fragment to stimulate antibody production. Applicant argues that examples of several biological activities are

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provided, however, the provided possible biological activities are merely exemplary, and are not a list of the only possible biological activities. As set forth above, many other biological activities can be ascribed to a peptide, and it would require undue experimentation for one of ordinary skill in the art to determine which biological activity is to be retained by the peptide for use in the claimed assay method.

Claims 11-12, 15-19, 24 stand rejected, and new claim 26 is rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in the Office Action of 10/30/2003. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The rejection of record set forth that these are genus claims. The claims are drawn to a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel, or a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a biologically active PCIP

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polypeptide fragment. Since the claims are directed to methods using biologically active fragments of PCIP 9q polypeptides, the claims encompass methods using variant proteins. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid deletions that may be made to the PCIP 9q fragment. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Applicant argues that the claimed genus is directed to specific fragments of PCIP molecules which are described in detail in the specification as filed. The claimed fragments are biologically active fragments of a 9q PCIP polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 16, 18, 20, 22, 24, 26, and 28, wherein said biologically active fragment is selected from the group consisting of an EF domain, residues 68-252 of human 9q and a potassium channel a subunit binding domain. However, the claims

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are directed to a method of identifying a compound that binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a biologically active PCIP polypeptide fragment. The term "biologically active" is not defined by the claims, and no definition is given as to what this activity is. Various biological activities can be attributed to a peptide. For example, "activity" could constitute transportation throughout a cell, alteration of tertiary structure due to changes in pH, ligand binding, or modulation of second messenger effect, etc. 'Activity' could also be referring to the ability of the fragment to stimulate antibody production. Applicant argues that there is sufficient written description in the Specification regarding the specific fragments of PCIP 9q. However, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, there is not a correlation between the structure of the fragments of PCIP polypeptides and the biological activity. While examples of several biological activities are provided, the possible biological activities are merely exemplary, and are not a list of the only possible biological activities. As set forth above, many other biological activities can also be ascribed to a peptide, and here there is not a correlation of any particular function to the fragment, thus the claims are not described.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-12, 15-19, 24, 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17-19 are vague and indefinite in the recitation of the term "biologically active". The term "biologically active" is not defined by the claim, but give no definition of what this activity is. Various biological activities can be attributed to a peptide. For example, "activity" could constitute transportation throughout a cell, alteration of tertiary structure due to changes in pH, ligand binding, or modulation of second messenger effect, etc. 'Activity' could also be referring to the ability of the fragment to stimulate antibody production. Claims 11-12, 15-16, 24, 26 are rejected insofar as they depend on the recitation of the term "biologically active".

Conclusion

Claims 1-3, 25 are allowable.

Claims 11-12, 15-19, 24, 26 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871.

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The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to be 'J. F. Murphy', with a long, sweeping horizontal stroke extending to the right.

Joseph F. Murphy, Ph. D.
Patent Examiner
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May 6, 2004